UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 15, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

10/30/98

MEMORANDUM

SUBJECT: **Phosmet**. (Chemical ID No. 059201/List A Reregistration Case No. 0242). HED Human Health Risk Assessment and Supporting Documentation for the Reregistration Eligibility Decision Document (RED). DP Barcode No. D236026.

FROM: Christina B. Swartz, Chemist
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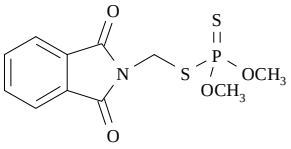
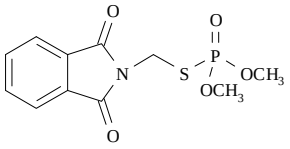
BACKGROUND

Phosmet [N-mercaptomethyl)phthalimide S-(O,O-dimethyl phosphorodithioate] is an organophosphate (OP) insecticide belonging to the phosphorodithioate subclass of organophosphates. Similar to other OPs, phosmet inhibits important nervous system enzymes known as cholinesterases (ChE). Phosmet is marketed for both occupational (agricultural and nonagricultural) and homeowner uses to control pests including moths, beetles, weevils, lice, flies and ticks. Products containing phosmet are formulated into dusts, emulsifiable concentrates, wettable powders and treated articles (i.e., flea collars). Phosmet and its metabolite, phosmet oxygen analog (phosmet oxon) [*N*-(mercaptomethyl) phthalimide *S*-(O,O-dimethyl phosphorothioate)], are the regulated residues of toxicological concern [refer to 40 CFR §180.261 (a) and (b)].



Phosmet



Phosmet oxon

Based on uses supported through reregistration, human health risk is associated with potential

exposure to phosmet and phosmet oxon through consumption of treated crops, livestock commodities and drinking water; in residential settings; and in occupational settings. The HED risk assessment addresses exposure in the diet and in residential settings (i.e., homeowner uses and residential post-application exposure from occupational uses). In addition, a comprehensive occupational risk assessment has been completed.

In conjunction with the human health risk assessment for phosmet, HED scientists have completed the following:

Hazard Identification Committee Report: George Ghali, Ph.D., 12/19/97
Toxicology Chapter of the Reregistration Eligibility Decision Document: William Greear, 1/7/98
The ORE Aspects of the HED Chapter of the RED: Jeff Dawson, 5/12/98
Product and Residue Chemistry Chapters of the HED RED: Christina Swartz, 6/18/98
Anticipated Residues for Chronic Non-Cancer Exposure Assessment: David Hrdy, 7/17/98
Acute/Chronic Dietary Exposure/Risk Analyses for the HED RED: Christina Swartz, 10/9/98

Detailed information pertaining to the basis for the HED risk assessment, including the tolerance reassessment, is provided in the attached documents. In addition, an environmental risk assessment was completed by the Environmental Fate and Effects Division (EFED): Environmental Fate and Effects Division RED Chapter for Phosmet, dated 5/1/98. Relevant portions of the EFED chapter are summarized.

Following completion of the toxicology chapter, an acute delayed neurotoxicity study [OPPTS Guideline No. 870.6100] was submitted by the registrant and reviewed by HED (W. Greear memo dated 9/15/98). A probabilistic (Monte Carlo) analysis of acute (one day) dietary exposure to phosmet was submitted by Gowan (personal communication with Linda Werrell, SRRD, 10/16/98), but is not included in the current assessment. Finally, an acute neurotoxicity study [OPPTS Guideline No. 870.6200] has been submitted by Gowan, and is currently under review.

SUMMARY/CONCLUSIONS

Available data indicate acute dietary risk associated with exposure to phosmet exceeds the Agency's level of concern for the general US population and population subgroups including infants and children (1-6 year and 7-12 years); chronic dietary risk for the US population and various population subgroups is below the Agency's level of concern. The chronic dietary risk assessment was based on highly refined residue data (anticipated residues), including field trial and processing studies submitted by the registrant, percent crop treated information, and monitoring data generated by the US Department of Agriculture (USDA). The acute dietary risk assessment was somewhat refined, since anticipated residues were used for blended commodities such as juices and milk, and since percent crop treated information was incorporated for some of the high-consumption items such as stone and pome fruit. Further refinement of the acute dietary exposure and risk estimates is possible; the registrant has submitted a probabilistic (Monte Carlo) assessment, currently under review in HED.

Data used in the occupational and residential handler and post-application risk assessments include the Pesticide Handlers Exposure Database (PHED, Surrogate Table of 5/97), and the SOPs for Residential Exposure Assessment. Chemical-specific data were available to calculate exposure for residential handlers and for post-application exposure (both residential and occupational exposures associated with activities such as crop maintenance and harvesting). In modeling exposures, maximum application rates were assumed using a variety of equipment types, and reasonable assumptions were made with respect to the amount of product handled in a typical day (i.e., acres treated and number of pets handled.). The PHED data used in the occupational handler assessment were of medium or high quality, while PHED data used to estimate residential exposures were considered to be low quality. In general, the model assumptions and techniques used to estimate exposures are those typically used by the Agency, and are further supported in scientific literature.

In spite of the application of maximum possible mitigation options, exposure and risk for occupational handlers exceed the Agency's level of concern for 13 scenarios, some of which involve mixing, loading and applying wettable powders using airblast sprayers or fixed-wing aircraft, or flagging for aerial applications. The 13 handler scenarios for which risk exceeds the Agency's level of concern were generally either higher rate scenarios, or scenarios for which there were no data to assess exposures. Post-application re-entry intervals (REIs) were calculated for citrus (282 days), pears (60 days), grapes (43 days), and low row crops (29 days). HED notes that the calculated REIs differ from those proposed by the registrant.

Exposure and risk for residential handlers were below the Agency's level of concern for all but 3 scenarios which involved application using a low pressure handwand sprayer. **HED is most concerned with residential post-application exposure and risk.** The calculated margins of exposure (MOEs) for short-term exposure to adults and children following home garden applications were approximately 50 (acceptable MOE = 300) on the day of treatment, but increased to >300 after 30 days; post-application intermediate-term MOEs were approximately 100 following home garden applications. The Agency's level of concern for short- and intermediate-term risk is exceeded for children exposed to treated pets, with calculated MOEs of less than 9 for dermal and hand-to-mouth scenarios. However, it should be noted that highly conservative assumptions were used to estimate post-application exposures to children.

The additional safety factor of 3X retained in accordance with FQPA may be removed pending submission of a subchronic neurotoxicity study. Removal of the 3X factor would reduce the Agency's level of concern with respect to dietary and residential exposures. Since the estimated residential and acute dietary exposures and risks currently exceed the Agency's level of concern, an aggregate risk assessment (i.e., including dietary exposure from both food and water, and from residential sources) has not been completed. When residential and dietary exposures are refined, the Agency will conduct and aggregate risk assessment.

DATA REQUIREMENTS

Additional data requirements have been identified in the science chapters (see attachments):

Toxicology

The following studies must be submitted:

OPPTS Guideline No. 870.6200, Subchronic neurotoxicity
OPPTS Guideline No. 870.3200, 21-day dermal toxicity
OPPTS Guideline No. 870.2600, Dermal sensitization

Residue Chemistry

OPPTS Guideline No. 860.1300, Directions for Use: Label amendments are required.
OPPTS Guideline No. 860.1380, Storage stability data:
Data are required for phosmet oxon (oil seed or nut crop, forage crop, starchy vegetable crop).
OPPTS Guideline No. 860.1500, Crop Field Trials:
Geographically representative data are required to support uses on blueberry and cotton (cotton gin by-products); additional data are required to support the post-harvest use on sweet potato.

Occupational and Residential Exposure

Depending on risk mitigation options and negotiations, phosmet-specific handler studies may be required. In addition, phosmet registrants must develop a strategy to generate chemical-specific transferable residue data to be used in conjunction with the Agricultural Reentry Exposure Taskforce (ARTF) database. The registrants may be required to develop additional chemical-specific data in conjunction with the work of the Outdoor Residential Exposure Taskforce (ORETF).

DETAILED CONSIDERATIONS

TOXICOLOGY

The Agency's toxicology database for phosmet is incomplete, but can be used to conduct a human health risk assessment. The available data demonstrate the anti-cholinesterase activity of phosmet in various species, including rats, dogs, mice and monkeys. Phosmet causes dose-related inhibition in plasma, red blood cell (RBC) and brain cholinesterase (ChE) activity via the oral route of exposure for various durations. Clinical signs in rats and rabbits exposed to phosmet in the diet include tremors, ataxia, salivation, subdued mood, urinary incontinence, piloerection, unsteady gait, and irregular breathing. However, none of the studies submitted to EPA indicate changes in brain weight or histopathology.

The HED Hazard Identification Assessment Review Committee (HIARC) concluded that the studies submitted to EPA are not adequate to address the potential for increased susceptibility to infants and children, as required by the Food Quality Protection Act (FQPA) of 1996. Under FQPA, an additional tenfold margin of safety is applied in Agency risk assessments to account for potential increased susceptibility of infants and children to the toxic effects of pesticides. Agency scientists must consider the completeness of the data with respect to exposure and toxicity to infants and children in determining whether the safety factor should be retained, reduced or removed.

Studies submitted to EPA do not include comparative characterization of ChE inhibition in pregnant females and their offspring. Evidence of reproductive toxicity was manifested in reduced fertility and mating performance in the 2-generation reproduction study in rats. In addition, reduced testes and ovary weights and moderately decreased spermatogenesis were observed. However, available data indicate no evidence of developmental anomalies or abnormalities in the development of the fetal nervous system. The HIARC concluded that the data are insufficient to determine the need for a developmental neurotoxicity study (OPPTS GDLN No. 870.6300). Therefore, the Committee recommended that the additional safety factor required under FQPA not be removed but reduced to 3X, pending submission of acute and subchronic neurotoxicity studies. The FQPA Safety Factor Committee supported the HIARC recommendation to reduce the safety factor to 3X. The data gap for an acute delayed neurotoxicity study in hens has been satisfied; phosmet was negative for delayed neurotoxicity in hens. However, the acute neurotoxicity and required subchronic neurotoxicity studies must be reviewed before HED will revisit the need for an FQPA Safety Factor. When these studies have been evaluated, the Agency will determine the need for a developmental neurotoxicity study.

Meetings were conducted to assess consistency in selecting endpoints and safety factors for all organophosphate pesticides; HIARC conclusions pertaining to endpoint selection and the FQPA Safety Factor for phosmet were supported. However, application of the safety factor in occupational and residential exposure assessments has changed (refer to the summary documents, "Hazard Assessment of the Organophosphates: Report of the HIARC" and "FQPA Safety Factor Recommendations for the Organophosphates," B. Tarplee and J. Rowland, 7/7/98 and 8/6/98, respectively). The conclusions are discussed in the relevant sections below.

Supporting documents refer to the NOEL (no observed effect level) and LOEL (lowest observed effect level) in toxicology studies. In order to harmonize with other offices in EPA, and to express greater clarity in scientific decision-making, OPP/HED has decided to use the terms no-observed-*adverse*-effect-level (NOAEL) and lowest-observed-*adverse*-effect-level (LOAEL) [policy memorandum, M. Stasikowski, 9/22/98]. The new policy is reflected in the current risk assessment, but not in the supporting documents.

Table 1. Acute Toxicity Profile

OPPTS GDLN	MRID	Study Type	Species	Results	Tox Category
870.1100	00046189	Acute Oral	rat	LD_{50} = 113 mg/kg (females and males)	II
870.1200	00046190	Acute Dermal	rabbit	LD_{50} = >5000 mg/kg	IV
870.1300	00063197	Acute Inhalation	rat	LC_{50} = >0.152 mg/L [No death occurred]	II
870.2400	00046192	Acute Eye Irritation	rabbit	Moderate Irritant	III
870.2500	00046191	Acute Skin Irritation	rabbit	No Irritation	IV
870.2600	N/A	Skin Sensitization	N/A	Data Gap	N/A

TOXICITY ENDPOINTS

The toxicological endpoints for risk assessment are summarized in Table 2 and discussed below.

Table 2. Toxicological Endpoints for Risk Assessment.[1]

EXPOSURE SCENARIO	NOAEL (mg/kg/day)	ENDPOINT (LOAEL, mg/kg/day)	STUDY	UNCERTAINTY FACTORS[2]
Acute dietary aRfD = 0.011 mg/kg/day	1.1	Plasma/RBC ChE Inhibition at 2-4 weeks (1.8)	Chronic Rat	100X (Conventional) 3X (FQPA)
Chronic dietary RfD = 0.011 mg/kg/day	1.1	Plasma/RBC ChE Inhibition at 2-4 weeks (1.8)	Chronic Rat	100X (Conventional) 3X (FQPA)
Short-/Intermediate-Term dermal	1.1	Plasma/RBC ChE Inhibition at 2-4 weeks Use Dermal Absorption Factor of 10%	Chronic Rat	Residential: 100X (Conventional) 3X (FQPA) Occupational: 100X (Conventional)
Short-/Intermediate-Term inhalation	1.1	Plasma/RBC ChE Inhibition at 2-4 weeks Use Inhalation Absorption Factor of 100%	Chronic Rat	

[1] NOAEL = No Observed Adverse Effect Level; LOAEL = Lowest Observed Adverse Effect Level; ChE =

Cholinesterase; RBC = red blood cell (erythrocyte)

[2] Conventional UF of 100 includes 10X for inter-species extrapolation and 10X for intra-species variability; an FQPA safety factor of 3X was retained by the FQPA Safety Factor Committee based on available data. Note that the FQPA factor is not applied in occupational risk assessments.

Endpoints for Risk Assessment

A chronic toxicity/carcinogenicity study in rats was selected to establish endpoints for acute dietary, chronic dietary, and short- and intermediate-term residential and occupational (dermal and inhalation) risk assessments. The study was summarized in the HIARC report. Effects seen at the lowest observed adverse effect level (LOAEL) of 1.8 mg/kg/day included red blood cell (RBC) and serum cholinesterase inhibition; the dose selected for risk assessment was the NOAEL of 1.1 mg/kg/day. Even though the endpoint was selected from a long-term study, the study was deemed appropriate for acute dietary and short-term occupational and residential risk assessments since the effects were seen as early as 2-4 weeks; furthermore, doses used in the chronic study were lower than those used in the subchronic toxicity studies.

A two-generation reproductive toxicity study in rats was cited by the HIARC as a supporting study for the reference dose, in which serum and RBC cholinesterase inhibition were observed in the parents. The LOAEL for reproductive toxicity was 6.1 mg/kg/day based on decreased fertility, with a NOAEL of 1.5 mg/kg/day.

Although no clinical signs were observed in the chronic oral study in rats, tremors were observed in the parents in the reproductive toxicity study at 23 mg/kg/day (RBC ChE inhibition occurred at a dose of 1.5 mg/kg/day, while serum ChE inhibition occurred at 6.1 mg/kg/day). In a developmental study in rats, clinical signs were observed in maternal rats at a dose level of 15 mg/kg/day. Since cholinesterase inhibition was not measured in the developmental study, it is not possible to make a direct comparison of doses at which cholinesterase inhibition and clinical signs of toxicity are observed. Qualitatively, however, the results of the three studies suggest that clinical signs of toxicity would be expected to occur at significantly higher doses than the NOAEL of 1.1 mg/kg/day, which is the basis of the HED risk assessment (all exposure durations).

Conventional uncertainty factors (UFs) for dietary, occupational and residential risk assessments based on endpoints selected from studies conducted in laboratory animals include a factor of 10X for intra-species variability and a factor of 10X for inter-species extrapolation. The FQPA safety factor of 3X is applied only in dietary and residential risk assessments.

The reference dose is defined as the NOEL/UF. The acute and chronic reference doses (aRfD and RfD), not including the FQPA safety factor of 3X, are 0.011 mg/kg/day.

Carcinogenicity

Phosmet has been shown to be a potent direct-acting mutagen based on the results of *in vitro*

testing. However, *in vivo* studies in rats and mice indicate phosmet has a weak carcinogenic potency relative to its strength as a mutagen. The rat study indicated there were no tumors related to the doses administered, which were considered to be adequate based on systemic toxicity. In mice, there were statistical increases in the incidence of liver tumors in male and female mice; in addition, females had an increased incidence of mammary gland adenocarcinomas, which are considered to be a rare tumor type.

The HED Cancer Peer Review Committee (CPRC, meeting held 1/26/94, memo dated 5/25/94) struggled with the carcinogenic classification of phosmet (using the criteria established in the 1986 "Guidelines for Carcinogenic Risk Assessment"); arguments were presented for both a C and a D classification. The Committee's classification of phosmet as a Group C, or possible human, carcinogen was based primarily on the results in the mouse carcinogenicity study, but was supported by other information such as structural-activity comparison with dimethoate (another OP known to be both carcinogenic and mutagenic) and additional historical tumor data from the National Toxicology Program, which strengthened the significance of the tumors found in mice.

For risk assessment purposes, the CPRC recommended using the reference dose, rather than a cancer potency factor (Q_1^*); that is, the reference dose was deemed by the Committee to be protective of cancer and other chronic effects.

DIETARY EXPOSURE/RISK

Phosmet is used on a variety of fruits, vegetables and field crops, and is applied directly to cattle and swine. Although additional studies are required to support uses on certain crops, the residue chemistry database for phosmet is robust. Adequate plant and livestock (both oral and dermal) metabolism studies have been submitted. Phosmet is extensively metabolized in both plants and livestock. Phosmet and its oxon, the residues of toxicological concern, were identified but did not constitute a significant portion of the total residue in plant metabolism studies. In oral metabolism studies in poultry and ruminants, phosmet *per se* was identified at a very low level only in egg yolk. In dermal metabolism studies conducted on cattle and swine, phosmet was identified as the major residue in fat, and was found at lower levels in other tissues; phosmet oxon was not identified in cattle or swine tissues.

Reassessed tolerances for residues in most treated crops are based on field trial studies in which residues were detected in crops; however, tolerances for residues in nuts, cottonseed and potatoes are reassessed at the combined limits of quantitation (LOQs) for phosmet and its oxon. Tolerances for residues in meat, milk and meat by-products are also based on the combined LOQs for phosmet and the oxon; however, the tolerance for residues in fat is based on residues detected in fat in oral and dermal studies. No tolerances are required for residues in poultry [category 3 of 40 CFR §180.6(a)].

Highly refined residue data were used in HED's chronic dietary risk assessment for phosmet.

Monitoring data from the USDA Pesticide Data Program (PDP), in concert with the percent crop treated (%CT) data provided by the Biological and Economic Analysis Division (BEAD), were used to develop anticipated residues in apples/applesauce, pear, grapes, peaches, apricots, plums, nectarines, sweet peas, potatoes, sweet potatoes and milk. In addition, concentration factors derived from studies submitted to EPA were used to determine anticipated residues in juices and other processed fractions for these commodities.

USDA/PDP analyzed commodities for phosmet during 1993-1996; in general, the number of samples analyzed for each commodity ranged from approximately >300 to >600, with the exception of sweet corn, applesauce and tomatoes, for which approximately 150 samples were analyzed. For most commodities, the percentage of samples with detectable residues was <5-10%; in peaches, the percentage of samples with detectable residues increased from 9% in 1993 to 28% in 1996. The reassessed tolerance for residues in peaches is 10 ppm, but the maximum residue detected by PDP in any year was 1.7 ppm.

Anticipated residues were determined for other commodities (for which only field trail data or tolerance-level residues were available) using %CT and concentration or reduction of residues during cooking/processing; concentration/reduction factors were derived from processing studies submitted to EPA. Some refinements were made in the acute dietary exposure/risk assessment, in accordance with current HED policy. For example, although tolerance level residues were used for most commodities, anticipated residues were used for blended commodities such as juices and milk. In addition, the adjustment for %CT was made for some commodities by creating residue distribution files with values of 0 ppm for the untreated portion of the crop, and tolerance-level residues for the portion of the crop assumed to be treated. While the HED acute dietary exposure assessment is not an upper-bound (worst-case) estimate, additional refinements could be made using probabilistic techniques. The registrant has submitted a probabilistic (Monte Carlo) analysis of acute dietary exposure, which is currently under review in HED.

Generally, provided the percentage of the reference dose consumed is less than 100%, dietary risk is considered to be below the Agency's level of concern. Since the FQPA Safety Factor Committee recommended an FQPA safety factor be retained at 3X for phosmet, the percentage of the RfD consumed must be less than 33% in order for dietary risk to be below the Agency's level of concern. Based on the results of the DEEM™ analyses, chronic dietary risk associated with the uses supported through reregistration is below the Agency's level of concern; however, acute dietary risk exceeds the Agency's level of concern for the general US population and population subgroups including infants and children (ages 1-6 and 7-12 years). Dietary risk estimates are presented in Table 3.

Table 3. Summary of Acute and Chronic Dietary Risk for Phosmet, Expressed as a Percentage of the Reference Dose (RfD = chronic; aRfD = acute).[1]

Population Subgroup	Chronic Dietary Risk[2] (% RfD)	Acute Dietary Risk[3] (%aRfD, 99.9th percentile)
U.S. Pop - 48 states - all seasons	2	1396
All infants (<1 year)	2	2768
Nursing infants (<1 year)	<1	2360
Non-nursing infants (<1 year)	3	2608
Children (1-6 years)	4	2321
Children (7-12 years)	3	1420
Females (13-19 yrs/not preg. or nursing)	1	514
Females (13-50)	2	1092
Males (13-19 years)	2	553
Males (20+)	2	784

[1] The FQPA Safety Factor Committee recommended retention of the FQPA Safety Factor at 3X; therefore, dietary exposure of greater than 33 % of the chronic or acute reference dose (RfD or aRfD) exceeds the Agency's level of concern.

[2] The chronic dietary risk is based on highly refined anticipated residues, incorporating % crop treated information, monitoring data, and processing factors derived from submitted data.

[3] In accordance with HED policy, the 99.9th percentile of exposure (and its associated acute dietary risk) is reported, since the acute risk estimate is based on somewhat refined residues (i.e., anticipated residues in blended commodities and incorporation of percent crop treated information).

OCCUPATIONAL AND RESIDENTIAL EXPOSURE/RISK

Products containing phosmet are intended for use by individuals in the normal course of employment (i.e., they can be occupationally exposed); some products may be purchased and used by homeowners. In addition, occupational uses of phosmet can lead to general population exposures in a residential setting (e.g., veterinary uses on domestic pets). Exposures are typically addressed for those who are involved in the application of pesticides (handlers or applicators) and those who are exposed to pesticides but who have not directly used them (post-application exposures). Handlers include both the professional applicator and the homeowner who purchases and uses a product. Post-application exposures include agricultural harvesters or children playing

on a pesticide treated lawn or with a treated animal. The Agency anticipates that both handler and post-application exposures to phosmet occur, whether it is used in the occupational setting or by the homeowner.

Supported use patterns served as the basis for both occupational and residential exposure and risk assessments conducted by HED. Chronic scenarios, in which exposure occurs for at least 180 days/year, are not expected for phosmet. For occupational workers, short- and intermediate-term risk assessments were completed for both handler and post-application exposures. For residential scenarios, short-term risk assessments were conducted for handler exposures, while short- and intermediate-term risk assessments were conducted for post-application exposures. Post-application risk assessments were based on dermal exposure only, since significant post-application inhalation exposure is not expected.

In accordance with the HIARC recommendations, dermal doses were corrected using a 10% dermal absorption factor; 100% absorption was used for inhalation exposures; and acceptable margins of exposure (MOEs) were considered to be 100 for occupational populations and 300 for residential populations.

Occupational Exposure

Occupational populations are potentially exposed to phosmet while making applications or following application to fruit and nut tree crops; grapes; field, small fruit and vegetable crops; sweet potatoes (post-harvest); non-crop areas; evergreens; ornamentals; and pine seedlings. In addition, applications are made to cattle, swine, and pets (dogs and cats).

Handler Exposure and Risk

Handler assessments were completed for mixer/loaders preparing spray solutions using liquid and wettable powder formulations for ground-based and aerial applications as well as chemigation. Applicator (and combined mixer/loader/applicator) exposures were assessed for most commonplace equipment types including groundboom, airblast, aerial, and handheld equipment such as backpack sprayers, high pressure handwands, and right-of-way sprayers. Applicator exposures were also considered for animal dipping treatments (e.g., livestock and pets), collar use, direct animal applications, dusting equipment use, and pine seedling treatments for nursery propagation purposes.

Occupational handler exposure/risk assessments often indicate a need for risk mitigation in order to ensure adequately protective MOEs. There are three basic risk mitigation approaches considered appropriate for controlling occupational exposures. These include administrative controls, the use of personal protective equipment (PPE), and the use of engineering controls. Occupational handler exposure assessments are completed using a baseline exposure scenario and, if required, increasing levels of risk mitigation (PPE and engineering controls) to achieve an appropriate MOE.

The baseline clothing/PPE ensemble for occupational exposure scenarios generally consists of an individual wearing long pants, a long-sleeved shirt, no chemical-resistant gloves (exceptions pertaining to the use of gloves are noted), and no respirator. The first level of mitigation generally applied is PPE. For phosmet, PPE involves the use of an additional layer of clothing, chemical-resistant gloves, and a respirator. The next level of mitigation considered in the risk assessment process is the use of appropriate engineering controls which, by design, attempt to eliminate the possibility of human exposure. Examples of commonly used engineering controls include closed tractor cabs, closed mixing/loading/transfer systems, and water-soluble packets. The use of a tiered mitigation approach was used in the completion of the handler exposure/risk assessment for phosmet.

No chemical-specific handler exposure data were submitted in support of the reregistration of phosmet. As a result, either data from the *Pesticide Handlers Exposure Database (PHED V1.1)* or approaches detailed in the *Standard Operating Procedures for Residential Exposure Assessment* were used to complete the assessment for occupational handlers.

PHED was designed by a task force consisting of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association. PHED is a generic database containing voluntarily submitted empirical exposure data for workers involved in the handling or application of pesticides in the field, and currently contains data for over 2000 monitored exposure events. The underlying assumption supporting use of PHED data is that exposure to pesticide handlers can be calculated generically (based on the available empirical data), since exposure is primarily a function of the physical parameters of handling and application process (e.g., packaging type, formulation type, application method, and clothing scenario).

To ensure consistency in the risk assessment process, a surrogate exposure table that contains a series of standard unit exposure values for various occupational exposure scenarios has been developed using PHED (*PHED Surrogate Exposure Guide of May, 1997*). This guide serves as the basis for the phosmet exposure assessment. The standard exposure values (i.e., the unit exposure values included in the exposure and risk assessment tables) are based on the "best fit" values calculated by PHED. The model calculates "best fit" exposure values by assessing data distributions and then calculates a composite exposure value representing the entire body, ranging from the geometric mean to the median of the selected data set. Exposure values calculated using PHED are of varying quality. Data quality is assessed by considering the analytical aspects (e.g., recovery) and the design aspects of the data (e.g., number of available data points compared to guideline requirements) selected for the assessment. Each value used in the phosmet assessment has a distinct quality associated with it that is addressed in the characterization of exposures/risks.

In some instances, exposure levels were calculated using models that are described in the *Standard Operating Procedures for Residential Exposure Assessment.* These models have been used for occupational exposures because the theories of the models are applicable to both residential and occupational settings. For phosmet, the exposure scenarios that were modeled

with this approach include the veterinary uses such as dusting or dipping a dog.

Equipment type and the nature of mixing/loading operations generally define the exposure scenarios included in pesticide handler exposure/risk assessments. Application rate ranges and differences in cultural practice (e.g., acres or gallons applied per day vary based on crop) are also used to differentiate exposure scenarios. Given these parameters, fifty occupational handler scenarios were identified for phosmet. Exposures were calculated for phosmet handlers at all levels of risk mitigation. Mitigation was applied to specific scenarios as required until exposure and associated risk were below the Agency's level of concern, or until the options for risk mitigation were exhausted.

At the baseline clothing scenario, exposures for a vast majority of all scenarios were less than 1.0 mg/kg/day. In fact, exposures for all mixer/loaders using liquid formulations were less than 0.1 mg/kg/day. Applicator exposures for all scenarios ranged from the nanogram/kg/day range for veterinary uses up to a maximum level of 0.29 mg/kg/day (for a low pressure handwand direct livestock treatment scenario). Exposure levels for all common agricultural application methods were less than 0.1 mg/kg/day. The only scenarios where exposure levels exceeded the 1.0 mg/kg/day level were for open mixing operations involving wettable powders. In these scenarios, exposures ranged from 0.018 mg/kg/day up to a maximum level of 10.0 mg/kg/day when preparing for orchard airblast operations. At the baseline clothing level, occupational handler risk was below the Agency's level of concern for only 9 exposure scenarios (i.e., no mixer/loader scenarios, mostly direct animal treatments and other agricultural methods at lower rates).

Risk mitigation was applied in an attempt to reduce risk. When an assessment was completed for individuals wearing additional clothing layers (e.g., coveralls and gloves) and respirators (as appropriate), exposures were reduced for all scenarios. In fact, no exposure exceeded 0.6 mg/kg/day and exposures for most scenarios were much less than 0.1 mg/kg/day. The same pattern of exposures was identified where open mixing events involving wettable powder formulations accounted for the highest exposures (a maximum of 0.55 mg/kg/day when preparing for orchard airblast applications). Risks were below the Agency's level of concern for another 16 exposure scenarios after the application of appropriate clothing/PPE risk mitigation measures (i.e., all liquid mixer/loader, some direct animal treatments, other varied methods).

When the use of engineering controls such as closed tractor cabs and closed mixing/loading systems served as the basis for risk assessment, exposure levels for all pertinent scenarios were reduced to less than 0.06 mg/kg/day. Exposure and risk fell below the Agency's level of concern for an additional 12 exposure scenarios using engineering controls (i.e., most wettable powder mixer/loader and aerial scenarios including flaggers).

When appropriate risk mitigation options were applied, exposure and risks were below the Agency's level of concern for 37 of the 50 identified scenarios. Acceptable risk levels could not be attained for the remaining 13 exposure scenarios because either no pertinent data exist for addressing the scenario or an appropriate level of risk could not be achieved for the scenario (i.e.,

mostly higher rate and no data scenarios).

Four major input parameters are needed to complete handler risk assessments including unit exposure values specific to the application equipment and level of risk mitigation; application rate; amount that can be treated in a day; and toxicology parameters. No chemical-specific exposure data for handlers were submitted in support of the reregistration of phosmet. Therefore, either PHED or models described in the SOPs for Residential Exposure Assessment were used to complete the exposure assessment.

Because of the nature of the PHED data and the manner in which the data are statistically handled in the system, unit exposures range from the geometric mean to the median of the data set selected for analysis. Unit exposure values obtained from PHED are assigned a "level of confidence" based on the analytical quality of the selected data and the number of available data points (i.e., high, medium, or low confidence). The confidence levels essentially reflect exposure guideline requirements. For example, in a high confidence data set the analytical aspects of the study would meet guideline requirements and there would be an adequate number of data points. One parameter would be circumspect for medium quality data and both parameters would be circumspect for low confidence data.

In the phosmet exposure assessment conducted for handlers, data for most scenarios where PHED was used are considered to be either medium or high confidence. The level of refinement for scenarios based on the Residential SOPs is more difficult to assess because the models are essentially theoretical and the supporting data are not available. These models, however, are thought to be conservative estimates of exposure because the dose levels calculated for a single exposure pathway are generally orders of magnitude greater than available population-based biological monitoring data. Application rates used generally reflect the maximum application rate for each scenario. Maximum application rates are not always used, and are therefore considered to be a conservative input.

The daily treated parameter (e.g., acres or animals per day) is considered to be a reliable estimate of what can be done on a single, very productive day (i.e., an upper-bound estimate). For phosmet, the daily treated values used reflect standard inputs routinely used by the Agency. Based on these considerations, and on the use of a correction for dermal absorption, the handler assessments should generally be characterized as an upper-bound estimate of exposure; however, the estimated exposures should be considered reliable because of the quality of the PHED data used and the general conservative nature of the estimates calculated using the SOPs for Residential Exposure Assessment.

Post-Application Exposure and Risk

Significant post-application exposure scenarios identified for phosmet include: harvesting fruit and nuts, low row crops, and grapes; pruning, propping, and other maintenance activities for fruit and nut trees; lower exposure activities such as scouting, weeding, and crop thinning; and tree/ornamental transplant operations. Four representative post-application scenarios were developed by the Agency, including harvesting citrus, pears and low row field crops, and harvesting and maintaining grapes.

Chemical-specific dislodgeable foliar residue data were submitted for phosmet, conducted on citrus, grapes, and pears using a wettable powder formulation. The half-lives for phosmet on pear and grape leaves were found to be approximately 10 days, while the half life on citrus was found to be approximately 40 days. Phosmet oxon residues were analyzed and found to constitute less than 20 percent of the parent. All analyses were completed using combined residues of phosmet and the oxon.

Post-application exposures are typically calculated using transfer coefficients, which are task-based values used to estimate exposures, coupled with chemical-specific dislodgeable foliar residue dissipation data. Transfer coefficients can be thought of as a job- or task-based measure of exposure for personnel entering previously treated areas and performing a repetitive task. Transfer coefficients (ratios of exposure to dislodgeable foliar residue) are determined in studies where the exposure of personnel engaged in specific tasks is measured along with concurrent dislodgeable foliar residues. Chemical- and task-specific exposure data or transfer coefficients were not available to complete this assessment. As a result, the transfer coefficients used were based on default values, defined by exposures while harvesting tree crops, grapes and low row crops. Default transfer coefficient values were defined by the Agency after careful scrutiny of the scientific literature published by recognized experts in the field of pesticide exposure assessment (Popendorf and Fenske).

Absorbed phosmet dose levels for individuals entering a field on the day of treatment ranged from 0.077 mg/kg/day up to 1.4 mg/kg/day depending upon the exposure scenario, crop, and application rate. Exposures on the day of treatment were lowest for harvesting low row crops, increasing for grape harvesting/maintenance and pear harvesting to a maximum for citrus harvesting. For each of these crops, allowing reentry into a treated field on the day of treatment for the purposes of harvesting or other modeled agricultural activity is not acceptable (i.e., MOEs for all less than 14).

For post-application exposures and risk, engineering controls and PPE are not considered to be viable options for risk mitigation. The only viable option for mitigating post-application risk is the use of the restricted entry intervals (REIs) in which entry into treated fields is prohibited until the ambient environmental concentration is below the Agency's level of concern based on specific activities such as picking grapes all day. REI values calculated for all crops ranged from 29 days for harvesting low row crops to 282 days for citrus harvesting. Grape and pear harvesting REIs

were calculated to be 43 and 60 days after application, respectively.

Chemical-specific dislodgeable foliar residue (DFR) data on a variety of crops, conducted at application rates ranging from 1 to 15 lb ai/acre, served as the basis for the assessment; these studies were acceptable, and were incorporated into the post-application assessment using standard techniques. Generic transfer coefficients used to calculate post-application exposure are commonly used by the Agency. The general concept of the transfer coefficient technique for calculating exposures and the transfer coefficient values used in this assessment appear to have been well-established in the scientific literature by recognized researchers (Popendorf and Fenske). In accordance with Agency guidelines for acutely toxic compounds, the DFR data were generated at the highest rates for the respective crops.

The post-application exposure scenarios evaluated are likely to represent the highest post-application exposures associated with phosmet use. Further refinement or inclusion of additional exposure scenarios is not warranted at this time because the scenarios that have been modeled are known to be critical in the production of the identified crops (i.e., crops must be harvested).

Residential/General Population Exposures

Handler Exposure/Risk

Handler assessments were completed for individuals preparing and applying liquid spray solutions using both liquid and wettable powder formulations with a variety of handheld equipment, including low pressure handwand, backpack, and hose-end sprayers. Direct animal (i.e., pet) treatments such as dog dipping and collar use were also evaluated.

In residential settings, risk mitigation is not considered to be a viable option in the same manner that it is used in occupational settings (e.g., extra clothing and a respirator would never be viable on a modern homeowner label because of a lack of training and the ability to enforce such requirements). The only options that are considered viable are those inherent in the packaging and formulation such as single use or closed system/coupling products. Unfortunately, the current exposure data in PHED do not allow for evaluation of the manner in which these subtle product and packaging refinements impact exposure. Therefore, a single clothing scenario consisting of short pants and short-sleeved shirts was used to calculate exposures for residential handlers; this clothing scenario is thought to be representative of homeowner handlers.

Since there were no chemical-specific handler exposure data for phosmet, either data from the *Pesticide Handlers Exposure Database (PHED V1.1)* or approaches detailed in the *Standard Operating Procedures for Residential Exposure Assessment* were used to complete the assessment for residential handlers.

Based on application rates and techniques, seventeen residential handler scenarios were identified for phosmet. Exposures (absorbed dose value presented) for all scenarios were in the μg/kg/day

range with a maximum level of 19 μg/kg/day calculated for the use of a wettable powder formulation with a low pressure handwand. Handler exposure and associated risk were below the Agency's level of concern for all scenarios except 3 which were based on the use of a low pressure handwand sprayer.

The PHED data used in the residential handler assessment were the best available but are considered to be low to medium confidence data because of analytical quality issues and the number of data points. In general, maximum application rates were used in the assessment, which is considered to be a conservative assumption. The daily treated parameters (e.g., acres or animals per day) are reasonable estimates for typical residential settings, and are routinely used by the Agency. Based on these inputs and the 10% dermal absorption factor applied in the exposure assessments, residential handler assessments for phosmet are considered to be upper-bound estimates; however, the low quality of the PHED data used should not be discounted. For most scenarios, acceptable MOEs were calculated, and sometimes exceed the acceptable MOE by large percentages and even orders of magnitude. Therefore, the quality of the exposure data may not be as critical in the evaluation of residential handler exposure and risk.

Post-Application Exposure and Risk

A number of post-application exposure scenarios exist for phosmet in residential environments. Some significant residential exposure scenarios that have been identified include: harvesting homegrown fruit, maintenance of fruit trees, weeding and thinning of crops; tree/ornamental transplant operations; and contact with previously treated pets. Other exposure scenarios exist for the general population such as entry into a previously treated evergreen tree farm for harvest. Even though these scenarios are known to exist, the resulting exposures are expected to be similar to or less than other residential exposures. In order to assess post-application exposure and risk, four representative residential scenarios were developed for phosmet, including adults harvesting pears; children harvesting pears; toddlers after dermal contact with treated pets; and toddler dose attributable to hand-to-mouth behavior following contact with a treated pet.

Chemical-specific dislodgeable foliar residue (DFR) data described above for occupational post-application exposures were also used in the residential post-application exposure assessment. Similarly, task-based generic transfer coefficients were used to estimate exposures. Chemical- and scenario-specific exposure data were generated for phosmet in conjunction with the pear DFR dissipation data, and were deemed to be acceptable for regulatory purposes. Passive dosimetry techniques were used to monitor subjects engaged in activities intended to simulate homeowners maintaining pear trees and harvesting fruit. Study results were modified with an adjustment factor to calculate exposures to children engaged in similar activities. Standard approaches outlined in the SOPs for Residential Exposure Assessment were used to calculate dose levels attributable to contact from treated pets (i.e., dermal and hand-to-mouth).

The calculated absorbed dose level for adults engaged in 0.7 hours of pear tree maintenance and harvesting on the day of treatment is 0.024 mg/kg/day; the dose level calculated for children is

0.022 mg/kg/day. Since data indicate that phosmet is somewhat persistent in the environment ($t_{1/2}$ 10 days), dose levels were also calculated for a 30 day period after application. Average absorbed dose level for adults engaged in 0.7 hours of pear tree maintenance and harvesting 30 days after treatment is 0.0033 mg/kg/day while the average dose level for children is 0.0030 mg/kg/day.

The objective of pet treatments is to maintain an efficacious dose over a treatment interval. Since there are no chemical-specific data to support phosmet pet treatments, the SOPs for Residential Exposure Assessment were used to address this scenario. In the SOPs, no dissipation is assumed occur. However, for the purposes of this assessment, a minimal dissipation rate of 1 percent per day was used. The dose to toddlers attributable to dermal contact with treated pets is 0.17 mg/kg/day on the day of application, and 0.13 mg/kg/day 30 days after application. The toddler dose attributable to hand-to-mouth activity during contact with treated pets is 9.9 mg/kg/day on the day of application and 7.3 mg/kg/day 30 days after application.

In the residential setting, risk mitigation is not considered to be a viable option in the same manner that it is used in occupational settings (e.g., restricted entry intervals). The only regulatory actions available are the development of more refined data or modification of use patterns (e.g., alter application rates, remove certain uses, etc.). Based on the calculated doses, margins of exposure (MOEs) for residential post-application scenarios are all less than 7 (an acceptable MOE for residential exposures is 300).

Chemical-specific dislodgeable foliar residue (DFR) and exposure data were available to calculate the post-application exposures for residential pear activities. These studies were accepted by the Agency for use in exposure assessments using standard techniques established in the scientific literature by recognized researchers (Popendorf and Fenske).

The post-application dose levels calculated for toddlers resulting from dermal contact and hand-to-mouth activity are thought to be conservative because dose levels calculated for a single exposure pathway are generally orders of magnitude greater than indicated by available population-based biological monitoring data. Application rates used are generally the maximum application rate and little or no dissipation is considered. In addition, the models use overly conservative estimates for residue transfer and ingestion (e.g., 100 percent of material on the hand is transferred in each hand-to-mouth event). Even though the dose levels calculated for pet treatment scenarios are thought to be conservative, there are poisoning incidents associated with this use pattern. The residential post-application exposure scenarios represent the highest post-application exposures associated with phosmet use.

Based on incident reports for animals treated with EPA Reg. No. 773-79, EPA has recommended modification of the label to include applications to dogs only (i.e., to exclude applications to cats or other pets), and to avoid treating a specific breed, the Pomeranian. Pet deaths were reported in conjunction with use/misuse of the product.

PHOSMET IN GROUND AND SURFACE WATER

The water resource assessment conducted by the Environmental Fate and Effects Division (EFED) is summarized below. For details, refer to the Environmental Fate and Effects Division RED Chapter for Phosmet, dated 5/1/98. The drinking water level of comparison (DWLOC) for acute exposure to phosmet in drinking water is zero, since the acute exposure to residues in food alone exceeds the Agency's level of concern. Both chronic and acute DWLOCs will be calculated pending refinement of residential and acute dietary exposure to phosmet.

Available data indicate that phosmet and its oxon are not expected to pose a significant threat to ground water resources. The limited fate data available for the oxon indicate it does not contribute appreciably to the concentration of phosmet in ground and surface waters. Although phosmet has moderate mobility, it is susceptible to aerobic soil metabolism, with a half-life of 3 days. Monitoring data from the STORET system and the Pesticides in Ground Water Database (1981-1990) were reported in the EFED chapter; no phosmet residues were detected in water, with limits of detection (LODs) ranging from 0.1 to 10 parts per billion (ppb). Phosmet usage was reported in some, but not all, of the counties in which wells were monitored.

A preliminary ground water assessment was conducted using the Screening Ground Water model, SCI-GROW, which estimates "maximum" groundwater concentrations from application of pesticides to crops. Based on the assumptions made in the inputs to the model, the resulting ground water concentration is considered to be a high-end to bounding estimate of acute exposure. For phosmet, the high-end ground water concentration estimated by SCI-GROW is 0.4 ppb.

There is a potential for contamination of surface waters with phosmet, in the event of runoff-producing rain events within a few days to weeks post application. Physical properties of phosmet suggest it will enter surface water via dissolution in runoff and be adsorbed to suspended and eroding materials. Phosmet's persistence is expected to be greater in surface waters with higher residence times, such as lakes and reservoirs, than in streams and rivers; however, its persistence is also affected by factors such as pH and microbial activity. Surface water monitoring data reported to the STORET system (1978-1994) indicate the presence of phosmet in surface waters in association with known use areas. Although the data suggest phosmet does not exceed concentrations above the very low ppb range, reported incidences could not be correlated with use patterns, were collected randomly throughout the year, and were too limited to reflect the extent of surface water contamination.

Tier 2 surface water drinking water estimated environmental concentrations (EECs) were calculated using the PRZM 3.1 model of an agricultural field and the EXAMS 2.97.5 model for fate and transport in surface water (PRZM-EXAMS). Crop-specific surface water concentrations were estimated. For each crop, the scenarios chosen were expected to produce runoff at more than 90% of the sites where the crop is grown. Model simulations were made with the maximum application rates for all crops.

Surface water concentrations were reported as the one-in-ten year estimates for various time intervals, including the peak (1-day) concentration and overall means; these EECs are considered to be upper-bound estimates of surface water concentrations. Most peak EECs for phosmet were less than 30 ppb, ranging from <1 ppb for apples in OR to 29.9 ppb for cotton in MS. However, EECs for kiwi/CA and pears/OR were 137 and 140 ppb, respectively. Overall mean EECs ranged from 0.01 ppb for apples/OR to 1.0 ppb for pear/OR and kiwi/CA.

AGGREGATE EXPOSURE/RISK

In accordance with FQPA, EPA is required to aggregate exposure and concomitant risk from food, water, residential and other non-dietary sources. An aggregate exposure and risk assessment has not been conducted for phosmet since the residential and acute dietary components of the aggregate risk exceed the Agency's level of concern. HED will conduct an aggregate risk assessment when the relevant exposure estimates are refined (i.e., via incorporation of the probabilistic analysis of dietary exposure, chemical-specific studies for residential exposure, or risk mitigation). The Agency's level of concern with respect to dietary and residential exposure and risk may be reduced pending submission of outstanding toxicology data.